INWARD RECTIFIER, G-PROTEIN ACTIVATED, MAMMALIAN, POTASSIUM CHANNELS AND USES THEREOF

ABSTRACT OF THE DISCLOSURE

Compositions and methods are provided for producing functional mammalian inward rectifier, G-protein activated potassium channels (Kir3.0 channels). A channel is a multimeric protein comprising one or more Kir3.0 polypeptides, *e.g.* Kir3.1, Kir3.2, *etc.*, where the polypeptides may be from the same or different species. The functional channel has the distinctive features of an anomalous rectifier, in that it conducts inward but not outward K^+ current; it is blocked by low concentrations of extracellular Cs^+ or Ba^{2+}; and the conductance of the channel does not depend solely on voltage, but on $(E-E_K)$. The ability of the channel to conduct inward K^+ current is modulated by G-proteins, particularly G-proteins of the G_i/G_0 family. A number of mammalian cell surface receptors activate G-proteins as a consequence of specific ligand binding. The signal transduction from receptor to Kir3.0 channel is therefore coupled through G-protein intermediates.

The functional Kir3.0 channels are useful in drug screening assays directed to modulation of cellular electrophysiology. Nucleic acids encoding Kir3.0 polypeptides are useful for expression of the gene product, and for identification of homologous genes from other species, as well as other members of the same family of proteins. Expression of the nucleic acids in a heterologous cell, *e.g.* Xenopus oocyte, confers the ability to cause a change in potassium flow in response to G-protein activation.